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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,954	SCHMITZ ET AL.	
	Examiner	Art Unit	
	IQBAL H. CHOWDHURY	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7,9,11-17 and 26-30* is/are pending in the application.

4a) Of the above claim(s) *27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,7,9,11-17 and 26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 4, 7, 9, 11-17, 26-27 and 28-30 are currently pending.

In response to a previous Office action, a non-final action (mailed on October 15, 2009), Applicants filed a response and amendment on March 15, 2010, amending claims 1, 4, 7, 11-13, 16-17, and 26, cancelling claim 10, and adding new claims 28-30 is acknowledged. Claim 27 remain withdrawn as encompassing non-elected invention.

Claims 1, 4, 7, 9, 11-17, 26 and 28-30 are under consideration.

Applicants' arguments filed on March 15, 2010, have been fully considered and are deemed persuasive to overcome all of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Withdrawn-Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The previous rejection of claims 1, 7 and 9-17 under 35 U.S.C. 112, first paragraph on scope of enablement is withdrawn in view of amendment of claim 1. This rejection has been discussed at length in the previous office action. Claim 1 now recites "a nucleotide sequence encoding a polypeptide having at least 95% identity to the amino acid sequence of SEQ ID NO: 2".

Maintained-Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The previous rejection of claim 4 under 35 U.S.C. 112, first paragraph on scope of enablement is maintained. This rejection has been discussed at length in the previous office action. The rejection is maintained for the following reasons.

The specification, while being enabling for a process for preparing amino acid methionine in transgenic organism, wherein the process comprises introduction of a nucleic acid sequence of SEQ ID NO: 1 encoding a threonine-degrading protein i.e. threonine aldolase of SEQ ID NO: 2 from S. cerevisiae and further comprising a nucleic acid encoding lysine degrading enzyme, lysine decarboxylase of SEQ ID NO: 12 encoded by SEQ ID NO: 11 from S. cerevisiae, does not reasonably provide enablement for a process for preparing amino acids, wherein the process comprises introduction of a nucleic acid sequence encoding a polypeptide, which is 95% identical to SEQ ID NO: 2 having threonine-degrading activity and further comprising any lysine degrading enzyme having consensus sequence of $G[X]_4GIM[X]_{45}M[X]_2RK[X]_2M[X]_{11}GGXG[X]_3E[X]_2E[X]_3W$ (SEQ ID NO: 29), or $LG[X]_8LVYGG[X]_3GIMGXVA[X]_9G[X]_3GXIP[X]_{24}MHXRK[X]_2M[X]_6F[X]_3PGG$ $XGTXEE[X]_2E[X]_2TW[X]_2[X]_3KP[X]_4N[X]_3[X]_{14}F$ (SEQ ID NO: 30) from any source having minor structural feature. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, **to make and/or use** the invention commensurate in scope with these claims.

Claim 4 is so broad as to encompass a process for preparing amino acids, wherein the process comprises introduction of a nucleic acid sequence encoding a polypeptide, which is 95% identical to SEQ ID NO: 2 having threonine-degrading activity and further comprising any lysine degrading enzyme having consensus sequence of $G[X]_4GIM[X]_{45}M[X]_2RK[X]_2M[X]_{11}GGXG[X]_3E[X]_2E[X]_3W$ (SEQ ID NO: 29), or $LG[X]_9LVYGG[X]_3GIMGXVA[X]_9G[X]_3GXIP[X]_{24}MHXRK[X]_2M[X]_6F[X]_3PGG XGTXEE[X]_2E[X]_2TW[X]_2[X]_3KP[X]_4N[X]_3X]_{14}F$ (SEQ ID NO: 30) from any source having minor structural feature, which includes many lysine degrading enzyme as well as many mutants, variants and recombinants. Claims still read on using any nucleic acid having lysine degrading activity and the consensus sequence does not give any substantial structural feature of said consensus sequence of SEQ ID NO: 29 because said sequence has 73 unknown amino acids out of 87, which is enormously broad that does not provide any information to predict structural feature of the polypeptide having lysine degrading activity. Claims as written interprets any polypeptide, which comprises many mutants, variants and fragments having lysine degrading activity. One of ordinary skilled in the art would not know how to make the claimed invention without structural feature of the claimed nucleic acid molecule encoding polypeptide used in the claimed method which would require undue experimentation. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acid sequences encoding any lysine-degrading protein, which includes many mutants and variants used in the claimed method. However, in this case the disclosure is limited to the nucleotide and encoded amino acid

sequence of only one lysine degrading protein i.e. threonine aldolase of SEQ ID NO: 12 encoded by SEQ ID NO: 11 used in the claimed method.

Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a process for preparing amino acids, wherein the process comprises introduction of a nucleic acid sequence encoding a polypeptide, which is 95% identical to SEQ ID NO: 2 having threonine-degrading activity and further comprising any lysine degrading enzyme having consensus sequence of G[X]$_4$GlM[X]$_{45}$M[X]$_2$RK[X]$_2$M[X]$_{11}$ GGXG[X]$_3$E[X]$_2$E[X]$_3$W (SEQ ID NO: 29), or LG[X]$_9$LVYGG[X]$_3$GIMGXVA[X]$_9$G[X]$_3$GXIP[X]$_{24}$MHXRK[X]$_2$M[X]$_6$F[X]$_3$PGG XGTXEE[X]$_2$E[X]$_2$TW[X]$_2$[X]$_3$KP[X]$_4$N[X]$_3$[X]$_{14}$F (SEQ ID NO: 30) from any source having minor structural feature. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a process for preparing amino acids in a transgenic plant by introducing of a nucleic acid sequence encoding any lysine degrading protein, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Therefore, the rejection is maintained.

Withdrawn-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that

form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The previous rejection of Claims 1, 7, 14-16 and 26 under 35 U.S.C. 102(b) as being anticipated by Monschau et al. (Threonine aldolase overexpression plus threonine supplementation enhanced riboflavin production in Ashbya gossypii, Appl Environ Microbiol. 1998 Nov; 64(11): 4283-90, see IDS) is withdrawn in view of amendment of claim 1. Monschau et al. do not teach a process for producing amino acid such as methionine, homoserine or lysine in a transgenic plant, wherein said plant is transformed with a vector comprising a gene encoding an enzyme having threonine degrading activity.

New-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Monschau et al. (Threonine aldolase overexpression plus threonine supplementation enhanced riboflavin production in Ashbya gossypii, Appl Environ Microbiol. 1998 Nov; 64(11): 4283-90, see IDS).

The instant claims are drawn to a process for producing amino acid such as methionine, homoserine or lysine in transgenic organism including microorganism, wherein said microorganism is transformed with a vector comprising a gene encoding an enzyme having threonine degrading activity.

Monschau et al. teach a method of producing L-amino acid glycine in a fungal strain Ashbya gossypii comprising and overexpressing a gene encoding threonine aldolase from S. cerevisiae, which degrade threonine, which is 99.8% identical to SEQ ID NO: 2, inherently a threonine degrading enzyme because of such high level identity to threonine degrading enzyme, wherein the process produces riboflavin, which is the end product of L-amino acid glycine. Monschau et al. further teach culturing and isolating the cell, which meets the limitation of isolating L-amino acid. All microorganisms including filamentous fungus inherently produce L-amino acids including methionine, homoserine or lysine, as these amino acids are necessary for growth of said microorganism.

Therefore, Monschau et al. anticipate claims 29 and 30.

New-Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Monschau et al. (Threonine aldolase overexpression plus threonine supplementation enhanced riboflavin production in Ashbya gossypii, Appl Environ Microbiol. 1998 Nov; 64(11): 4283-90) as applied to claims 29 and 30 above, and further in view of Allen et al. (Glycine metabolism enzymes, US PGPUB 2002/0123118, publication 9/5/2002).

Monschau et al. teach a method of producing L-amino acid glycine in a fungal strain Ashbya gossypii comprising and overexpressing a gene encoding threonine aldolase from S. cerevisiae, which degrade threonine, which is 99.8% identical to SEQ ID NO: 2, inherently a threonine degrading enzyme because of such high level identity to threonine degrading enzyme, wherein the process produces riboflavin, which is the end product of L-amino acid glycine. Monschau et al. further teach culturing and isolating the cell, which meets the limitation of isolating L-amino acid. All microorganisms including filamentous fungus inherently produce L-amino acids including methionine, homoserine or lysine, as these amino acids are necessary for

growth of said microorganism. . Monschau et al. do not teach use of an E. coli as host cell for over expressing said threonine aldolase gene (threonine degrading enzyme).

Allen et al. teach an E. coli transformed and overexpressing threonine aldolase gene, which is involved in glycine metabolism, i.e. glycine synthesis (paragraph 0015 and Example 9).

By combining the teachings of Monschau et al. and Allen et al., it would have been obvious to one to ordinary skill in the art at the time of the invention was made to use a E. coli instead of fungal strain Ashbya gossypii as a host cell to express said threonine aldolase gene as taught by Allen et al. and use the method of producing L-amino acid as taught by Monschau et al. to arrive the claimed invention.

One of ordinary skill in the art would have been motivated to use E. coli instead of Ashbya gossypii because E. coli is well known for expressing heterologous gene expression, and L-amino acid production, which is cheap, easy to grow and well characterized microorganism for using in fermentation for large scale production of biologically important compound.

One of ordinary skill in the art would have a reasonable expectation of success because Allen et al. could successfully used an E. coli as a host cell for overexpressing threonine aldolase, a glycine metabolic enzyme in view of high level skill and expertise of one of ordinary skilled in the art.

Therefore, the above references render the claim 11 prima *facie* obvious to one of ordinary skill in the art.

Claims 1, 7, 9, 12-17, 26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Monschau et al. (Threonine aldolase overexpression plus threonine supplementation enhanced riboflavin production in Ashbya gossypii, Appl Environ Microbiol. 1998 Nov; 64(11): 4283-90) as applied to claims 29 and 30 above, and further in view of Allen et al. (Glycine metabolism enzymes, US PGPUB 2002/0123118, publication 9/5/2002).

Monschau et al. teach a method of producing L-amino acid glycine in a fungal strain Ashbya gossypii comprising and overexpressing a gene encoding threonine aldolase from S. cerevisiae, which degrade threonine, which is 99.8% identical to SEQ ID NO: 2, inherently a threonine degrading enzyme because of such high level identity to threonine degrading enzyme, wherein the process produces riboflavin, which is the end product of L-amino acid glycine. Monschau et al. further teach culturing and isolating the cell, which meets the limitation of isolating L-amino acid. All microorganisms including filamentous fungus inherently produce L-amino acids including methionine, homoserine or lysine, as these amino acids are necessary for growth of said microorganism. Monschau et al. do not teach use of a transgenic plant over expressing said threonine aldolase gene (threonine degrading enzyme).

Allen et al. teach a plant cell transformed and overexpressing threonine aldolase gene, which is involved in glycine metabolism, i.e. glycine synthesis and regenerating a plant from transformed plant cell, wherein the plants are corn plant (paragraph 15-17, Example 6-8, and claims 11, 13, and 15-18).

By combining the teachings of Monschau et al. and Allen et al., it would have been obvious to one to ordinary skill in the art at the time of the invention was made to use a plant cell instead of fungal cell Ashbya gossypii as a host cell to express said threonine aldolase gene as taught by Allen et al. and use the method of producing L-amino acid as taught by Monschau et al. to arrive the claimed invention.

One of ordinary skill in the art would have been motivated to use plant cell to regenerate to plant instead of fungal cell Ashbya gossypii because plant is well known for expressing heterologous gene encoding protein, and L-amino acid production, which is simple, easy to grow and for using plant for large scale production of biologically important compound.

One of ordinary skill in the art would have a reasonable expectation of success because Allen et al. could successfully used a plant cell to regenerate to plant, as a host cell for overexpressing threonine aldolase, a glycine metabolic enzyme in view of high level skill and expertise of one of ordinary skilled in the art.

Therefore, the above references render the claims 1, 7, 12-17, 26-27 and 28 prima *facie* obvious to one of ordinary skill in the art.

Conclusion

Status of the claims:

Claims 1, 4-5, 7, 9, 11-17, and 26-30 are pending.

Claim 27 is withdrawn.

Claims 1, 4, 7, 9, 11-17, and 26-30 are rejected.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1652 (Recombinant Enzymes)

/Richard G Hutson/
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